The Effects of Capsaicin-Induced Intraoral Mucosal Pain on Jaw Movements in Humans

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Aims: *To determine whether mucosal pain, evoked through a novel topical capsaicin model, has an effect on jaw movement and whether psychologic factors have an association with any pain-induced movement effects.* ***Methods:*** *Mandibular movement was recorded from 26 asymptomatic subjects during free opening and closing, resistant opening jaw movements, and free and standardized chewing, at baseline and in test sessions while the subjects were wearing a custom maxillary mouthguard coated with either capsaicin cream (pain group, 13 subjects) or placebo cream (control group, an additional 13 subjects). All subjects completed the Depression Anxiety Stress Scales (DASS) and the Pain Catastrophizing Scale (PCS). Statistical analyses were made with independent* t *tests and bivariate correlation analyses.* ***Results:*** *Capsaicin induced moderate pain in the pain group, but there were no significant differences between the two groups in the change of kinematic variables from baseline except for a significantly greater increase from baseline in the number of chewing cycles per second (chewing rate) for free (*t = *2.74,* P = *.011) and standardized chewing (*t = *2.10,* P = *.047) in the pain group compared with the control group. In the pain group, the DASS anxiety score was negatively correlated (*r = *–.70,* P = *.007), with the change of mean opening velocity from the baseline to the test session in the free opening task, and the DASS depression score was negatively correlated to the increase of chewing rate in the free chewing task from the baseline to the test session (*r = *–.56,* P = *.046).* ***Conclusion:*** *Capsaicin-induced mucosal pain resulted in a significant increase in chewing rate but had no effect on amplitude or velocity in opening/closing jaw movements and chewing. Anxiety and depression scores correlated negatively with velocity in free opening jaw movement and chewing rate, respectively.*
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Key words: capsaicin, intraoral, jaw movement, mucosal burning pain, pain adaptation model

The precise relationship between pain and motor activity (ie, movement and muscle activity) is still controversial.[1,2] The Pain Adaptation Model proposes that existing pain results in a reduction in the range and speed of movement so as to reduce further injury and promote healing.[3] However, this model does not provide an adequate explanation of all pain-motor activity interactions.[1,2,4]

Recently, two new models have been proposed.[1,2] The Integrated Pain Adaptation Model (IPAM) suggests that the highly variable pain experience between individuals,[5–7] as well as psychologic

variables, can influence muscle recruitment strategies.[1,8] Evidence has recently been provided for associations between some psychologic variables (ie, depression and stress)[9] and the amplitude and/or velocity of chewing. Hodges and Tucker[2] have proposed another model that incorporates changes in recruitment patterns.

There is extensive trigeminal literature describing the association between pain and jaw motor activities during experimental muscle pain induced by algesic chemical injection into, most commonly, the masseter muscle.[1,10–16] There is little information as to whether other types of orofacial pain, such as mucosal or bone pain, have similar effects on jaw muscle activity and jaw movement as observed with algesic chemical injections into the jaw muscles. However, there may be differences in the motor effects of deep muscle pain in comparison with mucosal pain. Previous studies[17,18] have been consistent with earlier findings[19] in the spinal system that noxious algesic chemical stimulation of the tongue muscle or temporomandibular joint (TMJ) resulted in greater central sensitization than for algesic chemical stimulation of facial skin. It has also been reported that patients with burning mouth syndrome, who therefore suffer intraoral mucosal pain, can also have a jaw dysfunction.[20,21]

Mucosal pain is a symptom in a significant proportion of the general population (approximately 1%),[22] and it is unclear whether mucosal pain has an effect on jaw movement in humans. Capsaicin, the pungent component of red peppers, was employed to evoke mucosal pain since it has been used in human experimental studies.[23–25] Capsaicin applied to the oral mucosa is an appropriate model of clinical mucosal pain. When applied topically to the oral mucosa in healthy subjects, capsaicin causes moderate pain[24,25] consistent with the mean levels of pain (mean ± standard deviation [SD], 52 ± 36 mm) in patients with burning mouth syndrome.[26] Capsaicin activates TRPV1 receptor channels on nociceptive afferents, which are implicated in clinical mucosal pain.[27,28] In addition, capsaicin also evokes a burning sensation, increased blood flow, primary and secondary hyperalgesia, and an enhanced sensitivity to noxious and innocuous stimuli,[29,30] manifestations commonly seen among patients with clinical mucosal pain.[31,32]

The motor effects proposed by the Pain Adaptation Model are thought to be mediated via local brainstem interneuronal connections between nociceptive afferents and jaw muscle motoneurones. Since the Pain Adaptation Model does not specify the origin of the nociceptive input to the trigeminal system, it is hypothesized that, as would be expected from the Pain Adaptation Model, capsaicin-evoked mucosal pain should result in a reduction in the amplitude and velocity of jaw movement during chewing and simple opening/closing jaw movements. In addition, given recent evidence for an association between some psychologic variables and jaw movements during chewing (see above), it is also hypothesized that psychologic variables will demonstrate an association with pain-induced effects on movement. Therefore, the aims of this study were to determine whether mucosal pain, evoked through a novel topical capsaicin model, has an effect on jaw movement and if psychologic factors have an association with any pain-induced movement effects.

Materials and Methods

Twenty-six asymptomatic subjects were recruited for this study. The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[33] were used to rule out signs and symptoms of TMD in all subjects. Furthermore, subjects were asked for any history of orofacial pain and were excluded as applicable. The subjects were age and sex matched into two groups—a pain study group (6 men, 7 women; mean age ± SD, 29.5 ± 4.9 years) and a control group (6 men, 7 women; mean age ± SD, 29.6 ± 3.4 years). Written informed consent was obtained from all participants, as was ethics approval from the Human Research Ethics Committee of the Sydney West Area Health Service and the University of Sydney Human Research Ethics Committee.

Mouthguard Preparation and Clutches

During the first appointment, a gypsum dental cast was obtained from a maxillary alginate impression. A soft mouthguard (120 × 2.0 mm; Erkoflex, Erkodent) was constructed to cover the palate and buccal mucosa to almost the depth of the sulcus. To avoid interference with each subject's jaw movements during tasks (see below), the occlusal surface of the mouthguard was removed with a scalpel. A pair of custom metal clutches to support the target frame of a jaw-movement tracking system (see below) was also constructed for each participant at this first appointment.

Psychologic Assessment Before Recording

On the day of the experimental recording, subjects first completed two questionnaires measuring their emotional state (Depression Anxiety Stress Scales [DASS-42])[34] and cognitions related to pain (Pain

Catastrophizing Scale [PCS]).[35] The DASS-42 is a set of three self-reported scales designed to measure the negative emotional states of depression, anxiety, and stress. Each DASS scale contains 14 items. All subjects rated each item from 0 (did not apply to me at all) to 3 (applied to me very much, or most of time). The total score for each of the three scales was calculated. The PCS is a 13-item self-report scale to indicate subjects' thoughts and feelings toward previous experiences of pain. Subjects were asked to rate each item from 0 (not at all) to 4 (all the time). The scores were summed.

Jaw-Movement Recording

An optoelectronic jaw-tracking system (JAWS3D, Metropoly) recorded jaw movement (sampling rate, 67 samples/s). This system consists of two major components:

- A pair of target frames, with each frame holding three light-emitting diodes (LEDs) to act as tracking references.
- A camera setup, consisting of three charged-coupled device cameras fixed on a rigid tubular frame with a quadrangular section, to record the movement of the LEDs.

On the experiment day, the custom-made metal clutches were temporarily attached to two or three maxillary and mandibular right anterior teeth. The target frames were then secured to the clutches. The frames were positioned at the side of face, parallel to the Frankfort horizontal plane. The midincisal point (ie, the point between the incisal edges of the mandibular central incisors) was chosen as the reference point and displayed as a moving dot visible to the subject on a video screen. The location of this dot provided visual feedback for the subject in tracking a computer-controlled target, a linear bank of LEDs that illuminated in sequence.[36]

Jaw Tasks

During the recording session, subjects were instructed to perform jaw tasks in the following sequence:

- Jaw postural position: Subjects were instructed to sit relaxed in a chair with their lips lightly touching without swallowing, talking, or tooth contact for 15 seconds.
- Free open and close vertical jaw movement (five trials): Subjects were instructed to move the position of the midincisal point dot on the screen to track a linear bank of target LEDs as closely and smoothly as possible. This set of target LEDs was positioned to the side of the trajectory of the midincisal point dot. The LEDs were illuminated in sequence by custom software.
- Resistant opening (five trials): Similar to free open and close vertical jaw movement but with the application of a force of 1 to 2 N from the subject's thumb during the opening phase. A load-and-force system (ELF 3.4, Teckscan) allowed the subject to monitor and control the magnitude of force applied. The rationale for performing this task was to provide a relatively standardized passive resistance for all subjects during the opening phase to provide another task for testing with the intraoral capsaicin-evoked pain.
- Free chewing (two trials, 15 seconds each): Natural chewing of gum on the right side.
- Standardized chewing (two trials, 15 seconds each): Chewing of gum on the right side while following the speed of illumination of a set of target LEDs that oscillated at 900 ms/chewing cycle. This standardized chewing sequence did not involve the subject moving the jaw to track a target but simply moved the jaw to follow the oscillation timing of a set of LEDs.

All tasks were completed during two sessions: the baseline and test sessions. The baseline session involved wearing only the mouthguard. During the test session, the subject wore the mouthguard with either 1% capsaicin cream (active ingredients are capsicum oleoresin, cream base, and PCCA emollient cream, purchased and mixed by the West Lindfield Pharmacy and Compounding Centre) (pain group) or placebo cream (PCCA emollient cream) (control group) on the inner buccal surface (mucogingival area).

All subjects were aware that they would be assigned to either the pain or the control group but were not told to which group they had been assigned. Once the cream had been applied, though, subjects quickly became aware.

Pain Induction and Assessment

For each subject in the pain group, intraoral mucosal burning pain was induced by placement of the mouthguard with 1% capsaicin cream on its inner buccal surface. Subjects marked their pain level on an 11-point numerical rating scale (NRS), where 0 was defined as "no pain at all" and 10 was "the worst pain imaginable" and their burning sensation level on another NRS scale (0 was "no burning sensation" and 10 was "worst burning sensation"). Subjects drew their pain areas on an outline picture

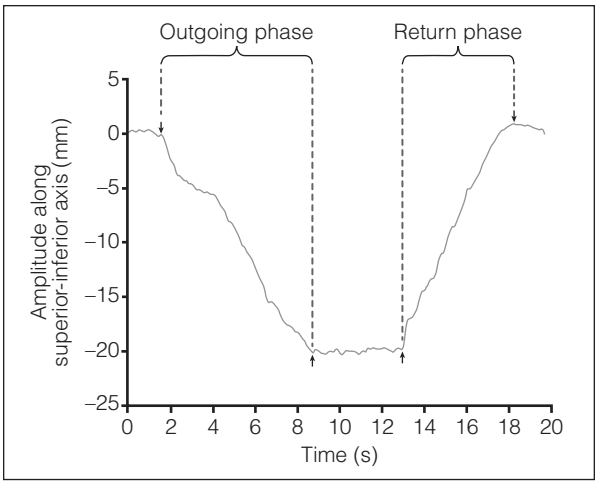

Fig 1 Plot of midincisal point tracing along the superior-inferior axis against time for a single opening/closing jaw movement. Vertical arrows define the beginning and end of each phase.

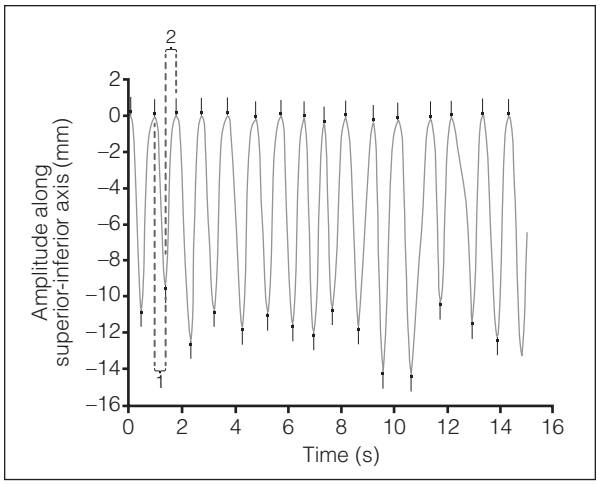

Fig 2 Plot of midincisal point tracing along the superior-inferior axis against time for a single free chewing movement in one subject. Vertical arrows define the maximum opening and closing of each cycle. 1, outgoing phase; 2, return phase.

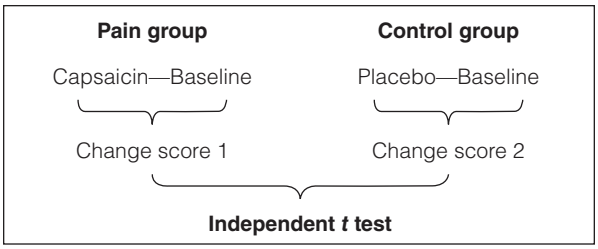

Fig 3 Data processing and analysis procedure. Baseline data were subtracted from the test data (ie, capsaicin/placebo).

of the head, neck, and oral cavity and completed a McGill Pain Questionnaire (MPQ)[37] to describe the quality of the pain.

Data Preparation

The ASCII files from the JAWS3D system were transformed into a Packing List file (PKL file), a type of Micromass file supporting multiple MS/MS datasets (Tandem Mass Spectrometry) by a customized computer program (Jaw Function Tool Kit, Faculty of Dentistry, University of Sydney). For each trial of free opening and closing jaw movement or resistant opening jaw movement (eg, see Fig 1), this software first identified an outgoing phase (along the superior-inferior axis, from the midincisal point displaced 0.5 mm from the jaw's postural position to the point at which the midincisal point was at maximal displacement) and a return phase (along the superior-inferior axis, from the point at which the midincisal point was at maximal displacement to the point at which the midincisal point was 0.5 mm from the postural position). The amplitude (mm) and velocity (mm/s) for the outgoing and return phases were calculated separately and averaged for each subject in each session (ie, baseline and test) over all trials of free opening and closing movement or resistant movement in that session. A similar analysis was carried out for free and standardized chewing movements in which the Jaw Function Tool Kit also identified the outgoing and return phases for each chewing cycle (Fig 2). Individual cycle and mean values were then calculated for absolute amplitude and velocity for free and standardized chewing in each session. The chewing rate for each subject for free and standardized chewing was also calculated by dividing the total number of chewing cycles in each trial by the corresponding time taken. A mean was then calculated for all trials for free or standardized chewing in that session. For each jaw task, the change score of the mean value of each kinematic variable between the baseline and test sessions was calculated for both the pain and control groups (Fig 3).

Data Analysis

Independent *t* tests were used to investigate significant differences between the two change scores for each kinematic variable (Fig 3). The Levene test was used to assess homogeinity of variance of change scores between the two groups. Bivariate correlation analysis investigated the relationship between psychologic variables and change scores of kinematic

Table 1 Scores for PCS and DASS Assessment

				Levene test for equality of variances		*t* test for Equality of Means					
	Group	n	Mean (SD)	*F*	Significance	*t*		*df*	Significance (two-tailed)	Mean difference	SE
PCS	Pain Control	13 13	8.15 (6.04) 12.62 (13.63)	5.30	.030	EV not assumed	–1.08	16.54	.296	–4.46	4.13
DASS depression	Pain Control	13 13	1.08 (1.75) 1.77 (2.86)	1.50	.232	EV assumed	–0.74	24.00	.464	–0.69	0.93
DASS anxiety	Pain Control	13 13	1.46 (1.33) 2.31 (4.37)	4.30	.049	EV not assumed	–0.67	14.21	.515	–0.85	1.27
DASS stress	Pain Control	13 13	3.15 (3.58) 3.54 (4.81)	1.45	.241	EV assumed	–0.23	24.00	.819	-0.38	1.66

PCS, Pain Catastrophizing Scale; DASS, Depression, Anxiety, and Stress Scales; EV, equal variances; *df*, degrees of freedom; SD, standard deviation, SE, standard error.

variables. $P < .05$ indicated statistical significance, and means and standard deviations (SDs) or standard errors (SEs) were calculated. The data were analyzed with SPSS 18.0 for Windows (IBM).

Results

DASS and PCS Scores, Pain Intensity, and Burning Sensation Intensity

There were no significant differences between the pain and control groups for the mean values of the PCS and DASS-42 scores (Table 1). The burning sensation intensity was strong (mean ± SD, 6.7 ± 1.6) and significantly greater than the moderate pain intensity (mean ± SD, 4.8 ± 1.5) for all pain subjects ($P = .004$). The NRS scores of pain intensity for each pain subject in all tasks during the test session are shown in Table 2. All subjects in the pain group localized the pain areas exclusively to the buccal gingival and alveolar mucosa, and there was no report of referral of pain to other intraoral areas or the face, head, neck, or other areas. However, the burning sensation spread to other oral regions in seven subjects: the middle of the palate in two subjects, the upper lips in three subjects, the tip of the tongue in three subjects (only one subject noted a burning sensation at both the lip and tongue). The MPQ pain rating index scores for its four categories were 7.31 (sensory), 1 (affective), 1.78 (evaluative), and 1.69 (miscellaneous). The most frequent words chosen by the pain subjects for each MPQ descriptor were "burning" (10 of 13) from the sensory word descriptors, "annoying" (6 of 13) from the evaluative descriptors, "punishing" (3 of 13) from the affective word descriptors, and "numb" (3 of 13) and "nagging" (3 of 13) from the miscellaneous word descriptors. Other commonly chosen words included "throbbing," "sharp," and "cruel."

Comparison of Changes of Mean Velocity and Amplitude of Jaw Movement from Baseline to Test Sessions Between Pain and Control Groups in All Tasks

For all tasks, there were no significant differences for the mean velocity and amplitude of jaw movement between the pain and control groups at baseline. There was significantly more variation in the changes from baseline of mean opening and closing amplitude during free opening in the pain group than in the control group (Levene test, Table 3). For all tasks, there were no significant ($P > .05$) differences in the changes of mean velocity and amplitude of jaw movement from baseline to test sessions between the pain and control groups (*t* tests in Tables 4 and 5).

Comparison of Chewing Rate Between the Pain and Control Groups

There were no significant ($P > .05$) differences between the control and pain groups for the chewing rate in either the free or standardized chew tasks at baseline. For the free chewing task, there was a significant difference ($P = .011$) between the two change scores from the baseline to the test session (increase of 0.12 cycles/s in the pain group and 0.01 cycles/s in the control group, *t* test for equality of means; see Table 5). For the standardized chew task, there was a significant difference ($P = .047$) between the two change scores from the baseline to the test session (an increase of 0.05 cycles/s in the pain group and a decrease of 0.01 cycles/s in the control group, *t* test for equality of means; see Table 5).

Table 2 NRS Score of Pain Intensity for All Pain Subjects in All Tasks During Test Session

		Free opening						Resistant opening					
Subjects	Start	T1	T2	T3	T4	T5	Mean	T1	T2	T3	T4	T5	Mean
1	5	7	6	6	6	6	6.2	5	5	5	5	5	5.0
2	5	5	6	6	6	5	5.6	5	4	4	4	4	4.2
3	4	4	4	4	4	4	4.0	4	4	4	4	4	4.0
4	4	4	4	4	4	4	4.0	4	4	4	4	4	4.0
5	3	3	3	3	3	3	3.0	3	4	3	2	2	2.8
6	4	4	4	4	4	4	4.0	4	5	4	4	4	4.2
7	4	5	5	5	4	4	4.6	4	4	4	4	4	4.0
8	4	4	4	4	4	4	4.0	4	4	4	4	4	4.0
9	3	3	1	1	1	1	1.4	1	1	1	1	1	1.0
10	2	2	3	3	3	3	2.8	3	3	3	4	3	3.2
11	3	5	5	4	1	3	3.6	4	4	4	4	4	4.0
12	3	3	2	2	2	2	2.2	2	2	2	2	2	2.0
13	3	3	3	3	3	3	3.0	3	3	3	3	3	3.0
Mean	3.6						3.7						3.5
SD	0.9						1.3						1.1

T, trial; NRS, numerical rating scale; SD, standard deviation.

Table 3 Comparison of Changes of Jaw Movement Mean Velocity (mm/s) and Amplitude (mm) from Baseline to Test Session Between Pain and Control Groups in Free and Resistant Opening

Changes from baseline to test				Levene test for equality of variances		*t* test for equality of means					
	Group	n	Mean (SD)	*F*	Significance	*t*		*df*	Significance (two-tailed)	Mean difference	SE
Free opening											
Velocity											
Opening	Pain	13	0.05 (0.47)	0.98	.331	EV	1.12	24.00	.272	0.19	0.16
	Control	13	–0.13 (0.36)			assumed					
Closing	Pain	13	0.02 (0.54)	3.82	.062	EV	0.99	24.00	.334	0.17	0.18
	Control	13	–0.15 (0.33)			assumed					
Amplitude											
Opening	Pain	13	–0.90 (3.11)	5.11	.033	EV not	–0.97	17.79	.343	–0.94	0.97
	Control	13	0.05 (1.58)			assumed					
Closing	Pain	13	–0.76 (3.49)	4.84	.038	EV not	–0.81	16.91	.431	–0.86	1.07
	Control	13	0.10 (1.62)			assumed					
Resistant opening											
Velocity											
Opening	Pain	13	–0.02 (0.53)	0.03	.868	EV	–0.09	24.00	.931	–0.02	0.22
	Control	13	0.00 (0.57)			assumed					
Closing	Pain	13	0.19 (0.54)	1.42	.245	EV	1.57	24.00	.130	0.29	0.18
	Control	13	–0.10 (0.38)			assumed					
Amplitude											
Opening	Pain	13	–0.09 (1.89)	1.14	.297	EV	–0.93	24.00	.360	–0.80	0.86
	Control	13	0.72 (2.46)			assumed					
Closing	Pain	13	0.11 (1.70)	1.81	.191	EV	–0.58	24.00	.566	–0.49	0.85
	Control	13	0.60 (2.54)			assumed					

df, degrees of freedom; SD, standard deviation; EV, equal variances; SE, standard error.

Free chewing			Standardized chewing			Peak pain
T1	T2	Mean	T1	T2	Mean	
5	5	5.0	5	4	4.5	7
4	5	4.5	4	4	4.0	6
3	3	3.0	2	2	2.0	4
4	4	4.0	4	4	4.0	4
2	3	2.5	3	3	3.0	4
5	4	4.5	4	4	4.0	5
3	3	3.0	3	3	3.0	5
3		3.0	—	—	—	4
1	1	1.0	1	1	1.0	3
3	3	3.0	3	3	3.0	4
7	7	7.0	7	7	7.0	8
5	5	5.0	5	5	5.0	5
2	2	2.0	2	2	2.0	3
		3.7			3.5	4.8
		1.6			1.6	1.5

Table 4 Comparison of Changes of Jaw Movement Mean Velocity (mm/s) and Amplitude (mm) from Baseline to Test Session Between Pain and Control Groups in Free and Standardized Chewing

Changes from baseline to test				Levene test for equality of variances		*t* test for equality of means	*t* test for equality of means			
	Group	n	Mean (SD)	*F*	Significance	*t*	*df*	Significance (two-tailed)	Mean difference	SE
Free chewing										
Velocity										
Opening	Pain	13	8.59 (6.22)	.41	.528	EV assumed	1.16	24.00	.258	2.64	0.16
	Control	13	5.96 (5.35)							
Closing	Pain	13	8.52 (8.29)	.98	.333	EV assumed	0.82	24.00	.419	2.44	0.18
	Control	13	6.07 (6.76)							
Amplitude										
Opening	Pain	13	1.69 (2.18)	.01	.941	EV assumed	–0.94	24.00	.357	–0.81	0.97
	Control	13	2.50 (2.23)							
Closing	Pain	13	1.67 (2.20)	.03	.864	EV assumed	–0.98	24.00	.338	–0.84	1.07
	Control	13	2.51 (2.19)							
Standardized chewing										
Velocity										
Opening	Pain	12*	3.48 (9.21)	3.95	.059	EV assumed	–0.96	23.00	.345	–2.73	0.22
	Control	13	6.21 (4.30)							
Closing	Pain	12*	4.61 (8.65)	3.79	.064	EV assumed	–0.52	23.00	.610	–1.45	0.18
	Control	13	6.06 (4.99)							
Amplitude										
Opening	Pain	12*	0.84 (3.55)	1.05	.317	EV assumed	–1.47	23.00	.155	–1.70	0.86
	Control	13	2.53 (2.10)							
Closing	Pain	12*	0.83 (3.53)	1.33	.260	EV assumed	–1.60	23.00	.124	–1.82	0.85
	Control	13	2.64 (2.00)							

df, degrees of freedom; SD, standard deviation; EV, equal variances; SE, standard error.
*In one subject of the pain group, the lower clutch detached from the teeth before the standardized chew for this subject was complete.

Table 5 Comparison of Changes of Chewing Rate from Baseline to Test Session Between Pain and Control Group in Chewing Tasks

Changes from baseline to test			Levene test for equality of variances		*t* test for equality of means			*t* test for equality of means		
Group	n	Mean (SD)	*F*	Significance	*t*		*df*	Significance (two-tailed)	Mean difference	SE
Free chewing										
Pain	13	0.12 (0.07)	2.64	.118	EV assumed	2.74	24.00	.011	.11	.04
Control	13	0.01 (0.13)								
Standardized chewing										
Pain	12*	0.05 (0.09)	1.90	.181	EV assumed	2.10	23.00	.047	.06	.03
Control	13	–0.01 (0.06)								

df, degrees of freedom; SD, standard deviation; EV, equal variances; SE, standard error.
*In pain group, because of saliva, one subject's lower clutch detached from the teeth and could not be reattached. Therefore, standardized chew for this subject was not completed.

Correlations Between Psychologic Variables and Changes of Kinematic Variables Between the Baseline and Test Sessions

In the pain group, a higher DASS anxiety score was related (r = –.70, P = .007) to a smaller increasing change (or bigger decreasing change) of mean opening velocity from baseline to the test session in the free opening task. In the control group, a higher DASS depression or DASS anxiety score was correlated with a smaller increasing change (or bigger decreasing change) of mean closing velocity from the baseline to test session in the free chewing task (DASS depression: r = –.56, P = .047; DASS anxiety: r = –.61, P = .026).

In the control group, the DASS stress score was positively correlated with the coefficient of variation for the mean opening (r =.71, P = .007) and closing velocity (r = .60, P = .030) in the baseline free chewing task. In the pain group, the DASS depression score was negatively correlated with the increase of chewing rate in the free chewing task from the baseline to the test session (r = –.56, P = .046).

Discussion

Main Findings

The main findings of the present study were that, compared with controls, experimental intraoral mucosal burning pain induced by capsaicin did not have a significant effect on the amplitude or velocity of jaw movement during opening/closing movements and during chewing but did result in a significant increase in the chewing rate during free and standardized chewing. Subjects with this type of experimental pain could achieve the same goal-directed jaw tasks as pain-free subjects. Correlations were noted between DASS anxiety, depression, and stress scores and some kinematic measures of jaw movement during chewing in the pain and control groups.

Pain Features

The capsaicin-evoked pain was moderate and was localized to the upper alveolar mucosa and buccal gingival margin and was associated with a strong burning sensation. The pain intensity was comparable to previous reports in humans of the intensity of experimental muscle pain evoked by hypertonic saline[10–12] and experimental orofacial cutaneous pain evoked by hypertonic saline[38] and experimental pain evoked by intra/perioral capsaicin.[24,25] Patients with burning mouth syndrome can experience similar mean levels of mucosal pain, although their worst pain intensity can be higher.[26]

The most common words chosen for each MPQ descriptor (sensory: "burning"; evaluative: "annoying"; affective: "punishing"; and miscellaneous: "numb") are similar to those words commonly chosen in previous studies applying capsaicin to other oral mucosal areas[39] and similar to the most frequent words chosen by patients with burning mouth syndrome pain.[27] However, the words are different from the most common words chosen following experimental orofacial cutaneous pain evoked by hypertonic saline (ie, "sharp"and "hot"[38]). Although the MPQ pain rating index scores of this experimental mucosal pain are comparable to those obtained during some previous experimental or clinical deep muscular pain studies,[10–12] the words chosen to describe capsaicin-induced mucosal pain are different from those words chosen in previous hypertonic saline-induced experimental muscle pain studies. For example, "aching" and/or "cramping" were the most frequent sensory word descriptors following masseter[15,38,40] and tibialis anterior[41] hypertonic saline

injections, while "exhausting" and "fearful" were the most frequent affective word descriptors.[15]

In contrast to masseter muscle pain evoked by hypertonic saline injections,[10–12] pain evoked by capsaicin was not associated with any pain referral, and the pain was quite localized to the upper gingival areas. The spread of the burning sensation to the upper lip, palate, and tip of tongue in seven subjects was likely due to a direct physical spread of the capsaicin cream.

Findings in Relation to Models of Pain-Motor Interactions

This is the first detailed description of the effects of mucosal burning pain on jaw movement. The findings that the activation of upper buccal mucosal nociceptors had only mildly significant effects on chewing jaw movements and no significant effects on goal-directed opening/closing jaw movements contrast with the literature, which reports effects of noxious stimuli on movement in both the trigeminal,[1,42,43] and spinal systems.[44] For example, reductions in the amplitude and velocity of movement, in comparison with pain-free controls, have been demonstrated in chronic low back pain patients[4,45]; TMD patients[46,47]; and experimental pain studies of gait,[45,48] trunk movement,[49] and mastication.[3,13,50,51]

The present findings that capsaicin-induced mucosal pain did not result in a significant reduction in amplitude or velocity of jaw movement during free and standardized chewing are not consistent with the Pain Adaptation Model, which proposes decreases in jaw movement amplitude and velocity in pain.[3] However, these findings are consistent with previous data demonstrating that hypertonic saline–evoked masseter muscle pain did not have a significant effect on jaw movement amplitude and velocity during free and standardized chewing.[15] The present findings suggest that these two different qualities of pain (mucosal versus muscular) have the same lack of significant effect on chewing amplitude and velocity.

However, the absence of a significant effect of capsaicin-induced mucosal pain on amplitude and velocity of jaw movement during single opening/closing movements is not consistent with previous studies demonstrating significant reductions in jaw-opening amplitude during the same single opening/closing movements during experimental masseter muscle pain[15] and reductions in movement amplitude and velocity in chronic musculoskeletal pain (eg, low back pain, fibromyalgia, and TMD).[3,42,46,52,53] Other studies have reported that topical capsaicin application to the tongue mucosa does not affect corticomotor pathways to the relaxed tongue musculature,[54] while noxious masseter or tongue muscle stimulation results in significant inhibitory effects on the primary motor cortex.[55–60] Further, noxious algesic chemical stimulation of the tongue muscle or temporomandibular joint (TMJ) results in greater central sensitization than for algesic chemical stimulation of facial skin.[17–19] Taken together, this suggests that noxious mucosal stimulation may not result in the same central sensitization effects along neuronal pathways, influencing jaw motoneurons as appears to occur with muscle pain.

It has been recently suggested in the IPAM that the features of the multidimensional pain experience may influence the effect of pain on motor activity.[1] Previous studies have demonstrated that experimental masseter muscle pain results in significant reductions in jaw-opening amplitude during single opening/closing jaw movements.[15] The present findings of no significant effects of mucosal pain on the same jaw movements provide tentative support for this proposal of the IPAM that some features of the multidimensional pain experience may influence the effects of pain on motor activity.

As mentioned above, this is a novel exploratory study with no estimate of treatment effects available in the literature. A sample size of 26 divided into two groups was sufficient to achieve an 80% power to detect an effect of 1.145 for each variable comparison. In the present study, it was decided to individually study each variable and condition. However, to investigate all the variables together and to reduce type II errors (false negative findings), a larger number of subjects in a future study would be needed.

Correlation Between Psychologic Variables and Kinematic Parameters

There is emerging evidence for a role for psychologic factors in the interaction between pain and motor activity.[1,5,61,62] Previous studies in the spinal[62–65] and trigeminal[9,66] systems provide evidence that depression, stress, catastrophizing, and/or fear avoidance correlate with objective measures of limb or jaw motor performance. Some associations were observed in the present study between depression, anxiety, or stress scores and chewing velocity, chewing rate, or variability in the pain or control groups. Further, the change of chewing rate between baseline and test of the mucosal pain subjects was significantly greater than that of the control subjects and may reflect motivational aspects—for example, a desire by the pain subjects to complete the task. Although these data are suggestive of possible associations between psychologic variables and movement features during mucosal nociceptive activation, the small sample size

and the acute nature of the pain in asymptomatic human subjects point to the need for further studies.

Conclusions

This is the first study to investigate possible relationships between experimental intraoral mucosal pain and amplitude and velocity of chewing and opening/closing jaw movements in a highly controlled manner. The present study has developed a methodology that allows testing of previous models of pain-motor interactions with another type of nociceptive input—namely, noxious mucosal stimulation. In comparison with the control group, mucosal pain resulted in only a small but significant increase in the chewing rate. This increase was negatively correlated with DASS depression scores. The absence of a significant reduction in single opening/closing jaw movements in mucosal pain contrasts with previous experimental and clinical muscle pain studies.

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References

1. Murray GM, Peck CC. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:263-278.
2. Hodges PW, Tucker K. Moving differently in pain: A new theory to explain the adaptation to pain. Pain 2011; 152(3, suppl):S90–S98.
3. Lund JP, Donga R, Widmer CG, Stohler CS. The pain-adaptation model: A discussion of the relationship between chronic musculoskeletal pain and motor activity. Can J Physiol Pharmacol 1991;69:683–694.
4. van Dieen JH, Selen LPJ, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. J Electromyography Kinesiol 2003;13:333–351.
5. Fillingim RB. Individual differences in pain responses. Curr Rheumatol Rep 2005;7:342–347.
6. Wiesenfeld-Hallin Z. Sex differences in pain perception. Gend Med 2005;2:137–145.
7. Shinal RM, Fillingim RB. Overview of orofacial pain: Epidemiology and gender differences in orofacial pain. Dent Clin North Am 2007;51:1–18.
8. Peck CC, Murray GM, Gerzina TM. How does pain affect jaw muscle activity? The Integrated Pain Adaptation Model. Aust Dent J 2008;53:201–207.
9. Brandini DA, Benson J, Nicholas MK, Murray GM, Peck CC. Chewing in temporomandibular disorder patients: An exploratory study of an association with some psychological variables. J Orofac Pain 2011;25:56–67.
10. Turp JC, Schindler HJ, Pritsch M, Rong Q. Antero-posterior activity changes in the superficial masseter muscle after exposure to experimental pain. Eur J Oral Sci 2002;110:83–91.
11. Sohn MK, Graven-Nielsen T, Arendt-Nielsen L, Svensson P. Effects of experimental muscle pain on mechanical properties of single motor units in human masseter. Clin Neurophysiol 2004;115:76–84.
12. Sae-Lee D, Whittle T, Peck CC, Forte ARC, Klineberg IJ, Murray GM. Experimental jaw-muscle pain has a differential effect on different jaw movement tasks. J Orofac Pain 2008;22:15–29.
13. Svensson P, Arendt-Nielsen L, Houe L. Sensory-motor interactions of human experimental unilateral jaw muscle pain: A quantitative analysis. Pain 1996;64:241–249.
14. Svensson P, Houe L, Arendt-Nielsen L. Bilateral experimental muscle pain changes electromyographic activity of human jaw-closing muscles during mastication. Exp Brain Res 1997;116:182–185.
15. Sae-Lee D, Whittle T, Forte ARC, et al. Effects of experimental pain on jaw muscle activity during goal-directed jaw movements in humans. Exp Brain Res 2008;189:451–462.
16. Stohler CS, Ashton-Miller JA, Carlson DS. The effects of pain from the mandibular joint and muscles on masticatory motor behaviour in man. Arch Oral Biol 1988;33:175–182.
17. Yu XM, Sessle BJ, Hu JW. Differential effects of cutaneous and deep application of inflammatory irritant on mechanoreceptive field properties of trigeminal brain stem nociceptive neurons. J Neurophysiol 1993;70:1704–1707.
18. Dubner R, Ren K. Brainstem mechanisms of persistent pain following injury. J Orofac Pain 2004;18:299–305.
19. Wall PD, Woolf CJ. Muscle but not cutaneous C-afferent input produces prolonged increases in the excitability of the flexion reflex in the rat. J Physiol (Lond) 1984;356:443–458.
20. Grushka M, Ching V, Epstein J. Burning mouth syndrome. Adv Otorhinolaryngol 2006;63:278–287.
21. Bergdahl BJ, Anneroth G, Anneroth I. Clinical study of patients with burning mouth. Scand J Dent Res 1994;102: 299–305.
22. Shulman JD, Beach MM, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in US adults: Data from the Third National Health and Nutrition Examination Survey, 1988-1994. J Am Dent Assoc 2004;135:1279–1286.
23. Capra NF, Ro JY. Human and animal experimental models of acute and chronic muscle pain: Intramuscular algesic injection. Pain 2004;110:3–7.
24. Baad-Hansen L, List T, Jensen TS, Svensson P. Increased pain sensitivity to intraoral capsaicin in patients with atypical odontalgia. J Orofac Pain 2006;20:107–114.
25. Boudreau S, Romaniello A, Wang K, Svensson P, Sessle BJ, Arendt-Nielsen L. The effects of intra-oral pain on motor cortex neuroplasticity associated with short-term novel tongue-protrusion training in humans. Pain 2007;132: 169–178.
26. Svensson P, Kaaber S. General health factors and denture function in patients with burning mouth syndrome and matched control subjects. J Oral Rehabil 1995;22:887–895.
27. Yilmaz Z, Renton T, Yiangou Y, et al. Burning mouth syndrome as a trigeminal small fibre neuropathy: Increased heat and capsaicin receptor TRPV1 in nerve fibres correlates with pain score. J Clin Neurosci 2007;14:864–871.
28. Ban A, Marincsak R, Biro T, et al. Upregulation of transient receptor potential vanilloid type-1 receptor expression in oral lichen planus. Neuroimmunomodulation 2010; 17:103–108.

29. Malmberg AB, Mizisin AP, Calcutt NA, von Stein T, Robbins WR, Bley KR. Reduced heat sensitivity and epidermal nerve fiber immunostaining following single applications of a high-concentration capsaicin patch. Pain 2004;111:360–367.
30. Gazerani P, Andersen OK, Arendt-Nielsen L. Site-specific, dose-dependent, and sex-related responses to the experimental pain model induced by intradermal injection of capsaicin to the foreheads and forearms of healthy humans. J Orofac Pain 2007;21:289–302.
31. Speciali JG, Stuginski-Barbosa J. Burning mouth syndrome. Curr Pain Headache Reports 2008;12:279–284.
32. Raber-Durlacher JE, Elad S, Barasch A. Oral mucositis. Oral Oncol 2010;46:452–456.
33. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. J Craniomandib Disord 1992;6:301–355.
34. Lovibond PF, Lovibond SH. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995;33:335–343.
35. Sullivan MJL, Bishop S, Pivik J. The pain catastrophizing scale: Development and validation. Psychol Assessment, 1995;7:524–532.
36. Sae-Lee D, Wanigaratne K, Whittle T, Peck CC, Murray GM. A method for studying jaw muscle activity during standardized jaw movements under experimental jaw muscle pain. J Neurosci Methods 2006;157:285–293.
37. Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. Pain 1975;1:277–299.
38. Nash PG, Macefield VG, Klineberg IJ, Murray GM, Henderson LA. Differential activation of the human trigeminal nuclear complex by noxious and non-noxious orofacial stimulation. Hum Brain Mapp 2009;30:3772–3782.
39. Boudreau SA, Wang K, Svensson P, Sessle BJ, Arendt-Nielsen L. Vascular and psychophysical effects of topical capsaicin application to orofacial tissues. J Orofac Pain 2009;23:253–264.
40. Nash PG, Macefield VG, Klineberg IJ, Gustin SM, Murray GM, Henderson LA. Bilateral activation of the trigeminothalamic tract by acute orofacial cutaneous and muscle pain in humans. Pain 2010;151:384–393.
41. Henderson LA, Bandler R, Gandevia SC, Macefield VG. Distinct forebrain activity patterns during deep versus superficial pain. Pain 2006;120:286–296.
42. Svensson P, Graven-Nielsen T. Craniofacial muscle pain: Review of mechanisms and clinical manifestations. J Orofac Pain 2001;15:117–145.
43. Sessle BJ. Peripheral mechanisms of orofacial pain. In: Sessle BJ (ed). Orofacial Pain: From Basic Science to Clinical Management. Chicago: Quintessence, 2008:27–33.
44. Ro JY, Capra NF, Masri R. Effects of experimental muscle pain on muscle spindle sensitivtiy. In: Graven-Nielsen T, Arendt-Nielsen L, Mense S (eds). Fundamentals of Musculoskeletal Pain. Seattle: IASP, 2008:369–381.
45. Arendt-Nielsen L, Graven-Nielsen T, Svarrer H, Svensson P. The influence of low back pain on muscle activity and coordination during gait: A clinical and experimental study. Pain 1996;64:231–240.
46. Dworkin SF, Huggins KH, LeResche L, et al. Epidemiology of signs and symptoms in temporomandibular disorders: Clinical signs in cases and controls. J Am Dent Assoc 1990;120:273–281.
47. Tsolka P, Fenlon MR, McCullock AJ, Preiskel HW. A controlled clinical, electromyographic, and kinesiographic assessment of craniomandibular disorders in women. J Orofac Pain 1994;8:80–89.
48. Graven-Nielsen T, Svensson P, Arendt-Nielsen L. Effects of experimental muscle pain on muscle activity and co-ordination during static and dynamic motor function. Electroencephalogr Clinl Neurophysiol 1997;105:156–164.
49. Zedka M, Prochazka A, Knight B, Gillard D, Gauthier M. Voluntary and reflex control of human back muscles during induced pain. J Physiol (Lond) 1999;520:591–604.
50. Schwartz G, Lund JP. Modification of rhythmical jaw movements by noxious pressure applied to the periosteum of the zygoma in decerebrate rabbits. Pain 1995;63:153–161.
51. Westberg KG, Clavelou P, Schwartz G, Lund JP. Effects of chemical stimulation of masseter muscle nociceptors on trigeminal motoneuron and interneuron activities during fictive mastication in the rabbit. Pain 1997;73:295–308.
52. Stohler CS. Craniofacial pain and motor function: Pathogenesis, clinical correlates, and implications. Crit Rev Oral Biol Med 1999;10:504–518.
53. van Dieen JH, Selen LP, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. J Electromyography Kinesiol 2003;13:333–351.
54. Halkjaer L, Melsen B, McMillan AS, Svensson P. Influence of sensory deprivation and perturbation of trigeminal afferent fibers on corticomotor control of human tongue musculature. Exp Brain Res 2006;170:199–205.
55. Adachi K, Murray GM, Lee JC, Sessle BJ. Noxious lingual stimulation influences the excitability of the face primary motor cerebral cortex (face MI) in the rat. J Neurophysiol 2008;100:1234–1244.
56. Nash PG, Macefield VG, Klineberg IJ, Gustin SM, Murray GM, Henderson LA. Changes in human primary motor cortex activity during acute cutaneous and muscle orofacial pain. J Orofac Pain 2010;24:379–390.
57. Farina S, Valeriani M, Rosso T, et al. Transient inhibition of the human motor cortex by capsaicin-induced pain. A study with transcranial magnetic stimulation. Neurosci Lett 2001;314:97–101.
58. Le Pera D, Graven-Nielsen T, Valeriani M, et al. Inhibition of motor system excitability at cortical and spinal level by tonic muscle pain. Clin Neurophysiol 2001;112:1633–1641.
59. Valeriani M, Restuccia D, Di Lazzaro V, et al. Inhibition of biceps brachii muscle motor area by painful heat stimulation of the skin. Exp Brain Res 2001;139:168–172.
60. Valeriani M, Restuccia D, Di Lazzaro V, et al. Inhibition of the human primary motor area by painful heat stimulation of the skin. Clin Neurophysiol 1999;110:1475–1480.
61. Madland G, Feinmann C. Chronic facial pain: A multidisciplinary problem. J Neurol Neurosurg Psychiatry 2001; 71:716–719.
62. Turner JA, Dworkin SF, Mancl L, Huggins KH, Truelove EL. The roles of beliefs, catastrophizing, and coping in the functioning of patients with temporomandibular disorders. Pain 2001;92:41–51.
63. Alschuler KN, Theisen-Goodvich ME, Haig AJ, Geisser ME. A comparison of the relationship between depression, perceived disability, and physical performance in persons with chronic pain. Eur J Pain 2008;12:757–764.
64. Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW. The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. J Behav Med 2007;30:77–94.
65. Thomas JS, France CR, Lavender SA, Johnson MR. Effects of fear of movement on spine velocity and acceleration after recovery from low back pain. Spine 2008;33:564–570.
66. Lobbezoo F, Trulsson M, Jacobs R, Svensson P, Cadden SW, van Steenberghe D. Topical review: Modulation of trigeminal sensory input in humans: Mechanisms and clinical implications. J Orofac Pain 2002;16:9–21.